

AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGAC
 CACGCCGACAGAAACTACTAAGGCCATCTCAGGGGTGCCTGTGCCAGGAGA
 GGGGGGCGGTGTCCCCGGGCCGAGAGCCATGCCTTTCGGCCTGAAGCTCCG
 CAGGACTCGGCGCTACAACGTCCTGAGCAAGAACTGCTTTGTTGCCCGGATC
 CGCCTGCTGGACAGCAATGTCATCGAGTGCACGCTGTCGGTGGAAGCACGG
 GGCAAGAGTGCCTGGAGGCCGTGGCCCAGAGGCTGGAGCTGAGGGAGACGC
 ACTACTTCGGCCTTTGGTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGTAGA
 GCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTG
 CTTTCTTCGGAGTCATGTTCTATGTGCCAAATGTGTACGGCTTCAGCAGGA
 GGCCACAAGATATCAGTATTACCTGCAAGTCAAAAAGACGTGCTTGAAGGA
 CGGTTGCGGTGCTCCCTGGAACAAGTGATCCGGCTGGCTGGCTTAGCTGTGC
 AAGCTGACTTCGGAGATTATAACCAGTTTGATTCCCAAGAGTTCCTCCGAGA
 GTATGTGCTCTTTCCTATGGATTTGGCCATGGAGGAGGCGGCTCTGGAGGAG
 CTAACCCAGAAGGTGGCCCAGGAACACAAAGCTCATAGCGGGATCCTGCCG
 GCTGAAGCTGAACTGATGTACATCAACGAGGTAGAGCGTTTGATGGATTTG
 GACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGG
 CATCTTCTTCATGGGGATTTTTGTGAGGAACAGGGTCGGGAGACAGGCAGTG
 ATATACAGGTGGAATGACATTGGGAGTGTTACTCACAGCAAAGCAGCCATCC
 TGTTGGAGCTGATTGACAAGGAGGAGACCGCGCTCTTCCATACAGATGATAT
 TGAAAATGCCAAGTACATTTCTCGGTTGTTTACCACTCGGCACAAATTTTACA
 AACAGAACAAGATCTGCACTGAACAGTCAAATTCTCCACCCCCAATCAGACG
 CCAGCCCACCTGGAGCCGGTCTCACTGCCAAGGCAGCAGCCGTATATCTTG
 CCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCATACTTCCCA
 AGACAGCATTTTCCCCGGGAACGAAGAAGCCTTGTAAGTCCGTTCTCACAAC
 AGCCTGGACCTTAATTACTTGAACGGCACCGTCAACCAATGGCAGCGTGTGCA
 GCGTTCACAGCGTCAACTCCCTCAGCTGCTCCAGAGCTTCATTCAGGCGTCT
 CCAGTGTCTTCCAACCTTAGCATCCCTGGGAGTGACATCATGAGGGCCGATT
 ACATCCCCAGCCACCGCCACAGCACCATCATCGTGCCGTCTTACAGGCCGAC
 CCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCTGATGCACGC
 AGACAGCCAGAGCCGGTCTCTGCGTAACCTCAATATCATCAACACCCATGCC
 TATAACCAGCCCGAGGAACTGGTGTACAGCCAGCCGGAGATGCGGGAGAGG
 CATCCCTACACGGTCCCCTATGCACACCAGGGGTGCTACGGTCACAACTTG
 TAAGTCCGTCTGACCAGATGAACCCCCAAAATTGTGCGATGCCTATCAAGCC
 AGGGGCCAGTTCCATCTCTCACACAGTGAGCACTCCAGAACTAGCCAACATG
 CAGCTCCAAGGAGCACAACACTATAGCACAGCCACATGCTCAAGAACTATC
 TATTCAGGCCGCCACCCCCCTTACCCTCGGCCCGTCCTGCCACCAGCACCCCA
 GACCTCGCCAGCCACCGCCACAAGTACGTACGCGGCAGCAGCCCTGATCTGG
 TAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACC
 TGTGGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCTCACAGCCACCAAG
 CACCATGGCGGGCGGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTG

FIGURE 1A

ATGAACAGCATGGTGAGAGGCATGGAGGCCATGACACTGAAGTCACTCAATA
 TCCCCATGGCTCGCCGCAACACCCTTCGGGAGCAGGGCCCTTCCGAGGAGAC
 GGGCGGCCACGAAGTGCACGGTCTCCCCAGTATCACCACAAGAAGACATTC
 TCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGAGGAGGAG
 ACCCTGGAGGCTGCACCTCAGGTTCTGTGCTTCGAGAGAAAGTAGAATACA
 GTGCCCAGCTGCAGGCTGCCCTGGCCCGCATCCCCAACAGGCCCCCACCTGA
 GTACCCAGGGCCAAGAAAAAGTGTGAGTAATGGGGCACTGAGACAGGACCA
 GGGAACCCCTCTTCCTGCCATGGCCAGGTGCAGGGTGCTGAGACACGGACCA
 TCCAAGGCCCTCAGTGTCTCCCGGGCAGAGCAGCTGGCTGTCAACGGTGCCT
 CTCTGGGTCCCTCCATCTCTGAGCCTGACCTAACCAGCGTGAAGGAGCGGGT
 CAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGTGAGAGATGTTCTCCCTGGAG
 GACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAAG
 ATGACGGGGCCCGCAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAAT
 GGGCTCTCGGTGGCCCGAGTGTGCGGGGCGGGAAGATGGTCGCCATGATGCCA
 CCGAGTCCCCATAGACGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAG
 ATGGAATGGTGTTCACAGAATATGAGCAGATTCCAAACAAAAAGGCCAACG
 GCGTCTTCAGCACCGCCACTCTGCCTGAGAACGCCGAGCGCAGCCGGATCCG
 AGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCCGACCAAAGAA
 AACAACACAGGCTATATCAACGCCTCCACATCAAGGTGGTGGTCGGCGGAT
 CAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGA
 CTTCTGGCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACT
 GCAGAGGAGGAGGGTGGACGGACCAAAAGCCATCGATACTGGCCCAAAGT
 GGGTCCAAGCATAGTTCTGCCACCTACGGCAAGTTCAAGGTCAACACAAAGT
 TCCGGACAGATTCTGGTTGCTATGCAACGACGGGCCTAAAGGTGAAGCACCT
 GCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGCAGTACACGGAAGTGGCCC
 CACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTGTCTACTTGGAGGAAA
 TCCAGTCAGTCCGACGCCACACCAACAGCGTGCTGGAAGGCATCAGGACCAG
 GCACCCCCCATCGTGGTTCACTGCAGCGCGGGTGTGGGAAGGACTGGTGTG
 GTTATCCTCTCTGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGG
 AGGTGCCCACGATGCTGCGATTCTCAGGGAGCAGAGGATGTTTCATGATCCA
 GACCATTGCGCAGTACAAGTTCGTCTACCAAGTCCTCGTCCAGTTCCTGCAGA
 ATTCCAGGCTCATTTGATCTCCTCCGGGATGCAGCTTCTGGAGGAGGGACGC
 AGCTCTGTCCTGCAGGGGGCGGCCACTTCGACAACATCTGCCTCCCCAGCC
 AGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATCA
 TGTATTATTTTATATAAGATAATTTATTTTTTCCCTCTTTGGAATAAGTTCTG
 TGAGTTATTATATAATGCTTCCCCCCCATACACACACAATAATATAGTGCT
 TCTCATTTG (SEQ ID NO:1)

FIGURE 1B

underlined = deleted in targeting construct

bold = sequence flanking Neo insert in targeting construct

AGCAGAGAGCCTGGTGGGCATGGACATCTTTATCCACATACCTTAGTGTGACCACGCCGA
CAGAAAACTACTAAGGCCATCTCAGGGGTGCCTGTGCCAGGAGAGGGGGGGCGGTGTCCCC
GGGCCGCAGAGCCATGCCTTTTCGGCCTGAAGCTCCGCAGGACTCGGCGCTACAACGTCCT
GAGCAAGAACTGCTTTGTTGCCCGGATCCGCCTGCTGGACAGCAATGTCATCGAGTGCAC
GCTGTCGGTGGAAAGCACGGGGCAAGAGTGCCTGGAGGGCCGTGGCCAGAGGCTGGAGCT
GAGGGAGACGCACTACTTCGGCCTTTGGTTTCTCAGCAAGAGCCAGCAGGCGAGATGGGT
 AGAGCTGGAGAAGCCACTGAAGAAACATCTGGACAAGTTTGCTAACGAGCCTCTGCTTTT
 CTTCGGAGTCATGTTCTATGTGCCAAATGTGTACGGCTTCAGCAGGAGGCCACAAGATA
 TCAGTATTACCTGCAAGTCAAAAAAGACGTGCTTGAAGGACGGTTGCGGTGCTCCCTGGA
 ACAAGTGATCCGGCTGGCTGGCTTAGCTGTGCAAGCTGACTTCGGAGATTATAACAGTT
 TGATTCCCAAGAGTTCTCCGAGAGTATGTGCTCTTTCCTATGGATTGGCCATGGAGGA
 GGCGGCTCTGGAGGAGCTAACCCAGAAGGTGGCCAGGAACACAAAGCTCATAGCGGGAT
 CCTGCCGGCTGAAGCTGAAGTATGATGACATCAACGAGGTAGAGCGTTTGGATGGATTGG
 ACAGGAGATCTTCCCCGTGAAGGACAGTCATGGCAACAGCGTGCACCTCGGCATCTTCTT
 CATGGGGATTTTTGTGAGGAACAGGGTCGGGAGACAGGCAGTGATATACAGGTGGAATGA
 CATTTGGGAGTGTTACTCACAGCAAAGCAGCCATCCTGTTGGAGCTGATTGACAAGGAGGA
 GACCGCGCTCTTCCATACAGATGATATTGAAAATGCCAAGTACATTTCTCGGTTGTTTAC
 CACTCGGCACAAATTTTACAAACAGAACAAGATCTGCACTGAACAGTCAAATTTCTCCACC
 CCAATCAGACGCCAGCCACCTGGAGCGGTCCTCACTGCCAAGGCAGCAGCCGTATAT
 CTTGCCTCCCATGCATGTCCAGTGCAGTGAGCACTACTCGGAGACCCACTTCCCAAGA
 CAGCATTTTCCCCGGGAACGAAGAAGCCTTGTAAGTGCCTTCTCACAACAGCCATGGACCT
 TAATTACTTGAACGGCACCGTCACCAATGGCAGCGTGTGCAGCGTTCACAGCGTCAATC
 CCTCAGCTGCTCCCAGAGCTTCATTACAGGCGTCTCCAGTGTCTCCAACCTTAGCATCCC
 TGGGAGTGACATCATGAGGGCCGATTACATCCCCAGCCACCGCCACAGCACCATCATCGT
 GCCGTCTTACAGGCCGACCCCAGATTACGAGACGGTCATGAGGCAGATGAAGAGGGGTCT
 GATGCACGCAGACAGCCAGAGCCGGTCTCTGCGTAACCTCAATATCATCAACCCCATGC
 CTATAACCAGCCCCGAGGAAGTGGTGTACAGCCAGCCGGAGATGCGGGAGAGGCATCCCTA
 CACGGTCCCCCTATGCACACCAGGGGTGCTACGGTCACAACTTGTAAGTCCGTCTGACCA
 GATGAACCCCCAAAATTGTGCGATGCCTATCAAGCCAGGGGCCAGTTCCATCTCTCACAC
 AGTGAGCACTCCAGAACTAGCCAACATGCAGCTCCAAGGAGCACAACACTATAGCACAGC
 CCACATGCTCAAGAACTATCTATTACAGGCCGCCACCCCTTACCCTCGGCCCCGTCTGC
 CACCAGCACCCAGACCTCGCCAGCCACCGCCACAAGTACGTACGCGGCAGCAGCCCTGA
 TCTGGTAACTCGGAAGGTGCAGCTCTCCGTAAAGACCTTCCAGGAGGACAGCTCACCTGT
 GGTCCATCAGTCTCTGCAGGAGGTGAGCGAACCCCTCACAGCCACCAAGCACCATGGCGG
 CGGCGGTGGCACGGTGAATAAACGCCACAGCCTGGAGGTGATGAACAGCATGGTGAGAGG
 CATGGAGGCCATGACACTGAAGTCACTCAATATCCCCATGGCTCGCCGCAACACCCTTCG
 GGAGCAGGGCCCTTCCGAGGAGACGGGCGGCCACGAAGTGCACGGTCTCCCCAGTATCA
 CCACAAGAAGACATTCTCGGATGCCACCATGCTGATCCACAGCAGTGAGAGCGAGGAAGA

FIGURE 2A

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GGAGGAGACCCTGGAGGCTGCACCTCAGGTTCTGTGCTTCGAGAGAAAGTAGAATACAG
TGCCCAGCTGCAGGCTGCCCTGGCCCCGCATCCCCAACAGGCCCCACCTGAGTACCCAGG
GCCAAGAAAAAGTGTCAGTAATGGGGCACTGAGACAGGACCAGGGAACCCCTCTTCCTGC
CATGGCCAGGTGCAGGGTGCTGAGACACGGACCATCCAAGGCCCTCAGTGTCTCCCGGGC
AGAGCAGCTGGCTGTCAACGGTGCCCTCTCTGGGTCCCTCCATCTCTGAGCCTGACCTAAC
CAGCGTGAAGGAGCGGGTCAAGAAAGAGCCTGTGAAGGAAAGGCCGGTGTGAGAGATGTT
CTCCCTGGAGGACAGCATTATAGAGAGAGAGATGATGATCAGGAATCTAGAGAAGCAGAA
GATGACGGGCCCCGAGGCACAGAAGAGACCGCTGATGTTGGCAGCGCTGAATGGGCTCTC
GGTGGCCCGAGTGTGCGGGCGGGAAGATGGTCGCCATGATGCCACCCGAGTCCCCATAGA
CGAGAGGCTCAGAGCCCTGAAGAAGAAGCTGGAAGATGGAATGGTGTTCACAGAATATGA
GCAGATTCCAAACAAAAAGGCCAACGGCGTCTTCAGCACCGCCACTCTGCCTGAGAACGC
CGAGCGCAGCCGGATCCGAGAAGTTGTCCCATATGAGGAGAATCGAGTGGAGCTCATCCC
GACCAAGAAAAACAACACAGGCTATATCAACGCCTCCACATCAAGGTGGTGGTTCGGCGG
ATCAGAATGGCACTACATCGCCACCCAGGGGCCCTTGCCACATACGTGCCATGACTTCTG
GCAGATGGTGTGGGAGCAGGGGGTGAATGTGATCGCCATGGTCACTGCAGAGGAGGAGGG
TGGACGGACCAAAAAGCCATCGATACTGGCCCCAACTGGGGTCCAAGCATAGTTCTGCCAC
CTACGGCAAGTTCAAGGTCACCACAAAGTTCCGGACAGATTCTGGTTGCTATGCAACGAC
GGGCCTAAAGGTGAAGCACCTGCTGTCCGGGCAGGAGAGGACCGTGTGGCACTTGCAGTA
CACGGA CTGGCCCCACCACGGCTGTCCAGAAGACGTCCAAGGATTTTTGTCTACTTGGGA
GGAAATCCAGTCAGTCCGACGCCACACCAACAGCGTGCTGGAAGGCATCAGGACCAGGCA
CCCCCCCATCGTGGTTCCTGTCAGCGCGGGTGTGGGAAGGACTGGTGTGGTTATCCTCTC
TGAGCTCATGATCTACTGCCTGGAACACAACGAAAAGGTGGAGGTGCCACGATGCTGCG
ATTCTCAGGGAGCAGAGGATGTTTCATGATCCAGACCATTCGCGCAGTACAAGTTCGTCTA
CCAAGTCCTCGTCCAGTTCCTGCAGAAATCCAGGCTCATTTGATCTCCTCCGGGATGCAG
CTTCTGGAGGAGGGACGCAGCTCTGTCTGCAGGGGGCGGCCACTTCGACAACATCTGCC
TCCCCAGCCAGAGGTGGATGGCTGGCAGCAGGCAGAAGCCAGAGTTACTCACAAACATC
ATGTATTATTTTATATAAGATAATTTATTTTTTCCCTCTTTGGAATAAGTTCTGTGAGT
TATTATATAATGCTTCCCCCCCCATACACACACAATAATATAGTGCTTCTCATTTG

FIGURE 2B

Gene Sequence
Structure *

192 bp

Sequence Deleted

274 bp

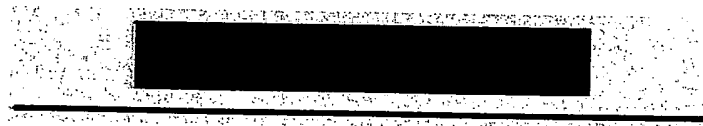
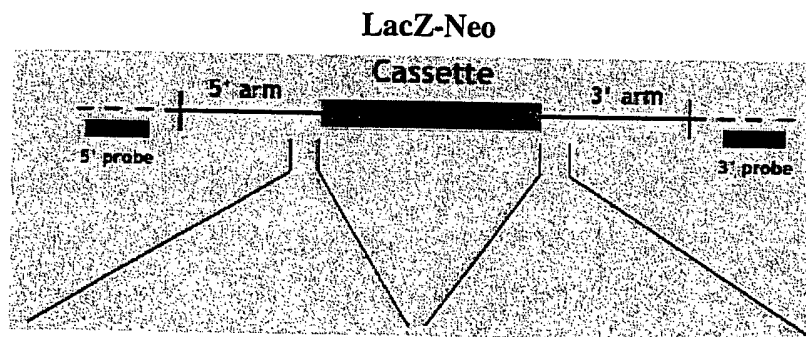
Size of full-length
cDNA: 3957 bp

FIGURE 3

Targeting Vector*
(genomic sequence)Arm Length:
5': 3.5 kb
3': 2 kb

— Targeting Vector
- - - Endogenous Locus

* Not drawn to scale

5' >CAGCTGCCCCGGCAGAGAGCCT
GGTGGGCATGGACATCTTTATCCA
CATACCTTAGTGTGACCACGCCGA
CAGAAACTACTAAGGCCATCTCA
GGGGTGCCCTGTGCCAGGAGAGGGG
GGCGGTGTCCCCGGGCCGAGAGC
CATGCCCTTTCGGCCTGAAGCTCCG
CAGGACTCGGCGCTACAACGTCCT
GAGCAAGAACT<3' (SEQ ID
NO: 2)

5' >GAGGCCGTGGCCCAGAGGCTG
GAGCTGAGGGAGGTGAGTTGAGCG
CGCATCCCTGCCTGTTGTGTGGAC
AGGGAGTGGGCTCTTCAGAGGAAC
CAGCTATCTGCTTAACGTGTTGGC
ACCTGCTGTGTTTTTCAGCCTAAGC
GTGTGTTTAAAGAACCTGCTTTT
CTTAGGGTGGGTGTGGCCCCGGGA
AGTTCCAGCAT<3' (SEQ ID
NO: 3)

FIGURE 4